REMARKS

Claims 1,2 and 4-7 are currently pending. Claim 1 has been amended. Support for the claim amendment can be found at page 7, lines 4-13 of the specification. The claim amendments and amendment to the specification are presented in a revised format per the USPTO's announcement 'Amendments in a Revised Format Now Permitted', dated 31 January 2002. Accordingly, a complete listing of all claims that are, or were in the application, along with an appropriate status identifier, is provided above in the section entitled "Amendments to the Claims".

Rejection under U.S.C § 101

Claims 1, 2 & 4-7 stand rejected under 35 U.S.C § 101 for lacking utility "because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility." Applicants respectfully traverse.

The Federal Circuit has stated, "[t]o violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result. MPEP § 2107.01 citing to" *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F. 2d 1555, 1571, 24 USPQ2d 1401, 1412 (Fed. Cir. 1992)(emphasis added). If an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on lack of utility is not appropriate. See *In re Brana*, 51 F. 3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995).

Rejections under 35 U.S.C. 101 have been rarely sustained by federal courts. Generally speaking, in these rare cases, the 35 U.S.C. 101 rejection was sustained either because the applicant failed to disclose any utility for the invention or asserted a utility that could only be true if it violated a scientific principle, such as the second law of thermodynamics, or a law of

nature, or was wholly inconsistent with contemporary knowledge in the art. MPEP 2107.02 citing to, *In re Gazave*, 379 F. 2d 973, 978, 154 USPQ 92, 96 (CCPA 1967).

The claims of the present invention are supported by a specific utility, namely that the DRG11 polynucleotides and the proteins expressed thereby can be use to identify, by nuclear staining, a subset of sensory neurons , since DRG11 is expressed in a very specific subset of sensory neurons and not expressed in sympathetic ganglia. It is also expressed in the dorsal spinal cord and not in the ventral spinal cord. This differential expression pattern makes the DRG11 protein a significant marker for identifying certain cell types when studying neuronal development. See page 20, lines 1-8 and page32, lines 26-27. The test for utility is not whether there is a specific disease or a specific target, but as stated in In *re Brana*, if the invention is only partially successful at achieving a useful result, a rejection of the claimed invention as a whole based on lack of utility is not appropriate.

In addition, the fact that DRG11 expression is specific to a subset of nociceptive (pain perception), NGF-dependent sensory neurons makes the DRG11 protein an important marker in studying nociception and the neuronal pathways involved. The fact that DRG11 expression is restricted to the nervous system and it is expressed not only in trkA expressing neurons but also in the dorsal horn of the spinal cord (which is a region into which NGF-dependent sensory neurons project) makes the DRG11 protein an important marker in studying the connectivity between sensory neurons and their targets in the central nervous system. See specification at page 32, lines 1-6; page 33, lines 11-25. There have been many gaps in understanding the synaptology of neuronal pathways in the dorsal horn, so a novel protein that has specific expression in the dorsal horn as well as in the sensory neurons that send inputs to the dorsal horn will prove as an important marker to the one skilled artisan for further understanding in the area

of pain perception. See *Pain. A Central Inhibitory Balance Theory*, Mayo Clinic Proc. 1975 Dec; 50(12):685-90 (Abstract).

In addition, the importance of DRG11 in playing an important role in regulating some aspect of synapse formation between sensory neurons and their central targets has been substantiated by a subsequent publication authored by the inventor of the present application. See attached abstract Neuron. 2001 Jul 19; 31(1):4-6 *The paired homeodomain protein DRG11 is required for the projection of cutaneous sensory afferent fibers to the dorsal spinal cord.* In this publication it has been shown that DRG11 is required for the projections from nociceptive sensory neurons to their central targets in the dorsal horn of the spinal cord. Mice deficient in DRG11 display abnormalities in the spatio-temporal patterning of cutaneous afferent fiber projections to the dorsal, but not the ventral spinal cord. See specification at page 34, lines 18-24.

The specific differential expression pattern of DRG11 can also be exploited to gain insight into the phenotypes and behavior of specific cell types of the nervous system and of the developmental pathways involved in neurogenesis. DRG11 is a sensory neuron specific marker for identifying sensory neurons in the mammalian crest which up to now has proven difficult. See specification at page 2, lines 9-15. This is a substantial utility as would be recognized by one of ordinary skill in the art. For all of the foregoing reasons the utility rejection is improper.

Finally, the Examiner cites to *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966) and states that the instant application is analogous. The instant application is not analogous to *Brenner* in which a utility was assumed based on structural similarity to other compounds. Here, the present application finds its utility based on evidence provided throughout the specification and examples of the differential expression pattern of DRG11 in the sensory neurons and in the dorsal horn and how this differential expression pattern can be used to study neurogenesis. The

utility of the instant application is not based on an assumption as was the case in *Brenner*.

For all the foregoing reasons, the rejection is improper. Applicants respectfully request the withdrawal of the rejection.

Claims 1-2 &4-7 are rejected under 35 U.S.C. § 112, first paragraph.

The Examiner states that since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. For the reasons set forth above, Applicants respectfully traverse.

The methods and procedures for isolating, expressing and using DRG11 nucleic acids is described throughout the specification. Isolation of DRG11 is described by the combination of degenerate PCR amplification with differential hybridization (see specification at page 22, lines 20-24; pages 23-29; and page 30, lines 1-2). In situ hybridization studies for observing the differential expression pattern is described in the specification at page 30, lines 3-26; page 31 and page 32, lines 1-16. Nuclear immunoflourescence staining of DRG11 expression in postnatal dorsal root ganglion cultures using monoclonal antibodies directed against DRG11 protein is also described in the specification at page 32, lines 17-27, page 33-34 and page 35, lines 1-7. For all of the foregoing reasons one skilled in the art would know how to use the claimed invention. In addition, as discussed above, the cited claims do satisfy the utility requirements. Therefore, Applicants respectfully request that this rejection be withdrawn.

Claims 1 and 5-7 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. Applicants respectfully traverse.

The Examiner states that

> one of ordinary skill in the art cannot visualize what generic nucleic acid sequences are specifically encompassed by the current claims, nor could one visualize what constitutes generic sequences encompassed by these claims based solely on the written description of the single cDNA sequence of SEQ ID NO:1 and because no known or disclosed function exists for the encoded DRG11 protein(s) of the instant invention, what constitutes a functional allelic variant (as it relates to the hybridization products claimed) cannot be reasonably determined.

An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, *Purdue Pharma L.P. v. Faulding Inc.*, 230 F. 3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) and MPEP § 2163 (II) (3).

Claim 1 is no longer defined by hybridization to SEQ ID No. 1. Claim 1, from which all other claims depend, is now directed to an isolated cDNA or recombinant nucleic acid comprising a nucleic acid encoding a DRG11 protein, wherein said protein sequence is at least 70 % identical to SEQ ID No. 2 and is characterized by its natural expression in sensory neurons and dorsal horn neurons of the spinal cord and non-expression in non-neuronal cells, sympathetic neurons and ventricular neurons of the spinal cord. The description in the specification is clearly sufficient to demonstrate that applicants had the subject matter of claim 1 in his possession as of the filing of the present application.

For the reasons discussed above, Claims 1, 2 and 4-7 sufficiently set forth an adequate written description of the cDNA or recombinant nucleic acid encoding a DRG11 protein and therefore, the rejection under 35 U.S.C. § 112, first paragraph is improper. Applicants respectfully request the withdrawal of the rejection.

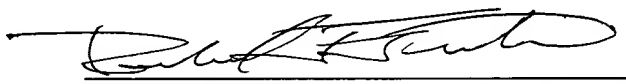
CONCLUSION

Applicants submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP

Dated: 4/30/03



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1: Mayo Clin Proc 1975 Dec;50(12):685-90 Related Articles, Links

Pain. A central inhibitory balance theory.

Kerr FW.

Knowledge of the segmental neuronal circuitry for noxious and non-noxious input is a necessary prelude to understanding pain mechanisms. Significant gaps in our understanding of the synaptology of these pathways in the dorsal horn have hindered progress in this area. This report describes the excitatory and inhibitory circuits that supply the marginal neurons of the spinal cord, whose role in nociceptive mechanisms is well established. On the basis of these data, it is proposed that large primary afferents (non-noxious) provide heavy inhibitory input to marginal neurons via gelatinosa cells. Conversely, small primary afferents (nociceptive) provide excitatory input to marginal neurons but relatively little inhibitory feedback to these cells via gelatinosa neurons. The modulation of pain-producing input depends thus on the balance between large-fiber and small-fiber activity via a postsynaptic inhibitory mechanism acting on the nociceptive relay neurons. This theory accounts satisfactorily for the modulation of pain by counterirritation and by various methods of stimulating large-fiber input.

Publication Types:
- Review

PMID: 172744 [PubMed - indexed for MEDLINE]

1: Neuron 2001 Jul 19;31(1):59-73 Related Articles, Links

Comment in:
- Neuron. 2001 Jul 19;31(1):4-6.

FULL TEXT @ CELL PRESS

The paired homeodomain protein DRG11 is required for the projection of cutaneous sensory afferent fibers to the dorsal spinal cord.

Chen ZF, Rebelo S, White F, Malmberg AB, Baba H, Lima D, Woolf CJ, Basbaum AI, Anderson DJ.

Division of Biology 216-76 and, Howard Hughes Medical Institute, California Institute of Technology, 91125, Pasadena, CA, USA.

Cutaneous sensory neurons that detect noxious stimuli project to the dorsal horn of the spinal cord, while those innervating muscle stretch receptors project to the ventral horn. DRG11, a paired homeodomain transcription factor, is expressed in both the developing dorsal horn and in sensory neurons, but not in the ventral spinal cord. Mouse embryos deficient in DRG11 display abnormalities in the spatio-temporal patterning of cutaneous sensory afferent fiber projections to the dorsal, but not the ventral spinal cord, as well as defects in dorsal horn morphogenesis. These early developmental abnormalities lead, in adults, to significantly attenuated sensitivity to noxious stimuli. In contrast, locomotion and sensori-motor functions appear normal. Drg11 is thus required for the formation of spatio-temporally appropriate projections from nociceptive sensory neurons to their central targets in the dorsal horn of the spinal cord.

PMID: 11498051 [PubMed - indexed for MEDLINE]